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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,314	08/19/2003	Rasappa G. Arumugham	ACY33317-D1	3547

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EXAMINER	
DEVI, SARVAMANGALA J N	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,314	ARUMUGHAM ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- Th MAILING DATE of this communication appears on the cover she t with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-23* is/are pending in the application.

4a) Of the above claim(s) *14-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *81903*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Preliminary Amendments

1) Acknowledgment is made of Applicants' preliminary amendments filed 08/19/03, 03/25/04 and 04/09/04. With these, Applicants have amended the specification.

Election

2) Acknowledgment is made of Applicants' election filed 03/25/04, of claims 19-23, equivalent to invention I set forth in the restriction requirement mailed 2/27/04. In response to the species election requirement, Applicants have elected the *N. gonorrhoeae* bacterial species and *N. meninigitidis* outer membrane protein carrier species. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P § 818.03(a)).

Applicants request for the acknowledgment of the preliminary amendment filed in August 2003. Applicants bring to the Office's attention the amendment filed in August 2003, which canceled claims 1-13 and presented new claims 19-23. As indicated below under 'Status of Claims', the preliminary amendment of August 2003 has been received, but was not matched with the case at the time the restriction requirement was mailed out. The Office regrets any confusion and/or inconvenience this may have caused to Applicants. Applicants are correct in equating the elected claims 19-23 to the subject matter of invention I, drawn to an antigenic conjugate, and claim 4 to claim 21 (carrier protein species) and claim 6 to claims 19 (Gram negative bacterial species). The restriction grouping as modified is set forth below:

I. Claims 19 through 23, drawn to an antigenic conjugate and an immunogenic composition comprising the same, classified in class 424, subclass 250.1.

II. Claims 14 through 18, drawn to a method of immunizing an individual and a method of preventing sepsis in a mammal, classified in class 514, subclass 898.

Claim 21 recites a plurality of structurally distinct carrier protein species: tetanus toxin or toxoid; diptheria toxin, toxoid or mutant of diptheria toxin CRMI97; *Pseudomonas* exotoxin A; cholera toxin or toxoid; Group A streptococcal toxins; pneumolysin of *Streptococcus pneumoniae*; filamentous haemagglutinin (FHA); FHA fragments of *Bordetella pertussis*; pili or pilins of *Neisseria gonorrhoeae*; pili or pilins of *Neisseria meningitidis*; outer membrane proteins of

Neisseria meningitides; outer membrane proteins of *Neisseria gonorrhoeae*; C5A peptidase of *Streptococcus;* or surface protein of *Moraxella catarrhalis*.

Claim 19 recites a plurality of disclosed structurally and genetically distinct gram negative bacterial species: *Neisseria gonorrhoeae*; *Haemophilus influenzae* non-typeable or *Haemophilus influenzae*; *Haemophilus ducreyi*; *Helicobacter pylori*; *Escherichia coli*; *Chlamydia*; *Salmonella*, *Salmonella typhimurium*, or *Salmonella minnesota*; *Proteus mirabilis*; *Pseudomonas aeruginosa*; *Moraxella catarrhalis*; *Bordetella pertussis*; *Shigella*; *Klebsiella*; or *Vibrio cholerae*.

Applicants have elected the bacterial species, *N. gonorrhoeae*, and the protein carrier species, *N. meninigitidis* outer membrane.

Status of Claims

3) Claims 1-13 have been canceled via the amendment filed 08/19/03.

New claims 19-23 have been added via the amendment filed 08/19/03.

Claims 14-23 are pending.

Claims 19-23 have been elected.

Claims 14-18 have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 19-23 are under examination. A First Action on the Merits is issued on these claims.

Information Disclosure Statement

4) Acknowledgment is made of Applicants' Information Disclosure Statement filed 08/19/03. The information referred to therein has been considered and a initialed copy is attached to this Office Action.

Priority

5) The instant application is a Divisional application of application SN 09/264,747, filed 03/09/1999, *now U.S. patent 6,645,503*, which claims priority to the provisional application, SN 60/088,364, filed 03/10/1998.

Specification

6) The instant specification is objected to for the following reason(s):

(a) The amendment introduced to the first paragraph of the specification does not reflect the issued status of a prior application, as shown above under 'Priority' in italicized letters. Amendment to the specification is requested.

(b) The use of the trademarks has been noted in this application. For example, see page 20, lines 15 and 18: "Tween 20"; page 17, line 20: "Biogel P30"; page 16, lines 15, 28 and 32 and page 17, line 12: "Biogel P6". The recitations should be capitalized wherever they appears and be accompanied by the generic terminology. Each letter of the trademark must be capitalized. See M.P.E.P 608.01(V) and Appendix I. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. It is suggested that Applicants examine the whole specification to make similar corrections to the trademarks, wherever such recitations appear.

Rejection(s) under Non-Statutory Double Patenting

7) The non-statutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970) and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 C.F.R 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See e.g., *In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir, 1985)*.

8) Claims 19-23 are rejected under the judicially created doctrine of obviousness-type double

patenting as being unpatentable over claims 1-7 of Arumugham *et al.* (US 6,645,503) ('503). Although the conflicting claims are not identical, they are not patentably distinct from each other, because the above-identified claims of the '503 patent are within the scope f the instant claims, since the recited structure of the conserved portion of the neisserial lipopolysaccharide in both sets of claims are identical.

Rejection(s) under 35 U.S.C. § 101

9) 35 U.S.C. § 101 states:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this cycle.

10) Claim 19 and claims dependent therefrom are rejected under 35 U.S.C. § 101 as being directed to a non-statutory subject matter. The claims read on a product of nature, i.e., for example, naturally occurring gonococcal cells comprising the LPS conserved portion, directly or indirectly conjugated to an endogenous protein. Claim 19 lacks limitations, which distinguish the product from those that may exist naturally. Consequently, the claim does not embody patentable subject matter as defined in 35 U.S.C § 101. See MPEP 2105. It is suggested that Applicants use a limitation, such as, --an isolated lipopolysaccharide (LPS)--, --a purified lipopolysaccharide (LPS)--, or --isolated and purified lipopolysaccharide (LPS)-- in connection with the LPS to reflect the hands of the inventors in the production or creation of the recited composition if descriptive support for such a limitation exists in the instant specification, as originally filed.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

11) Claims 19-23 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

New claim 19 includes the limitations: "the conserved portion of the lipopolysaccharide ... of ... *Neisseria gonorrhoeae, Haemophilus influenzae, nonptypeable Haemophilus*

influenzae, Haemophilus ducreyi, Helicobacter pylori, Escherichia coli, Chlamydia, Salmonella, Salmonella typhimurium, Salmonella Minnesota, Proteus mirabilis, Pseidomonas aeruginosa, Moraxella catarrhalis, Bordetella pertussis, Shigella, Klebsiella, and *Vibrio cholera*, wherein the conserved portion of the LPS comprises GlcNAc-Hep2-phosphoethanolamine-KDO_2-LipidA, wherein the conjugate elicits a 'cross protective' immune response against heterologous strains of gram negative bacteria". Applicants point to the originally filed claims and the specification, in particular to page 5, line 26 through page 7, line 2 of the specification as providing descriptive support for the new claim 19. However, this part of the specification neither describes a conserved portion of the LPS of *Neisseria gonorrhoeae, Haemophilus influenzae, nonptypeable Haemophilus influenzae, Haemophilus ducreyi, Helicobacter pylori, Escherichia coli, Chlamydia, Salmonella, Salmonella typhimurium, Salmonella Minnesota, Proteus mirabilis, Pseidomonas aeruginosa, Moraxella catarrhalis, Bordetella pertussis, Shigella, Klebsiella*, and *Vibrio cholera*, wherein the conserved portion of the LPS comprises GlcNAc-Hep2-phosphoethanolamine-KDO_2-LipidA, nor elicitation of 'cross protective' immune response by a conjugate comprising such a structure. While the limitation 'GlcNAc-Hep2-phosphoethanolamine-KDO_2-LipidA' is described in the first paragraph of page 15 and the last two paragraphs of page 8 of the instant specification, exclusively in connection with the LPS of *N. meningingitidis*, there is no descriptive support for such a conserved structure being present in all the Gram negative bacteria recited in the claim, either in a de-O-acetylated or non-de-O-acetylated form. Furthermore, the new limitation 'cross protective' does not appear in the instant application as originally filed. Therefore, the limitations in the claims are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to remove the new matter from the claim(s), or invited to point to specific pages and line numbers in the specification where support for such recitations can be found.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (Lack of Enablement)

12) Claims 19-23 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a lack of enablement rejection.

The claims are drawn to an antigenic conjugate and an immunogenic composition comprising the conjugate, wherein said conjugate comprises a carrier protein covalently bonded to the conserved portion of a LPS of *Neisseria gonorrhoeae, Haemophilus influenzae, nonptypeable Haemophilus influenzae, Haemophilus ducreyi, Helicobacter pylori, Escherichia coli, Chlamydia, Salmonella, Salmonella typhimurium, Salmonella minnesota, Proteus mirabilis, Pseidomonas aeruginosa, Moraxella catarrhalis, Bordetella pertussis, Shigella, Klebsiella*, and *Vibrio cholerae*, wherein the conserved portion of the LPS comprises GlcNAc-Hep2-phosphoethanolamine-KDO_2-LipidA, and wherein the conjugate elicits a 'cross protective' immune response against heterologous strains of gram negative bacteria. The claimed conjugate is required to comprise GlcNAc-Hep2-phosphoethanolamine-KDO_2-LipidA nd is required to elicit a 'cross protective immune response' against heterologous strains of any Gram negative bacteria. However, the instant specification lacks probative evidence enabling such an antigenic conjugate or an immunogenic composition comprising the same.

Instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;
- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant application, the claimed conjugate comprises the conserved portion of a LPS of *Neisseria gonorrhoeae, Haemophilus influenzae, nonptypeable Haemophilus influenzae,*

Haemophilus ducreyi, Helicobacter pylori, Escherichia coli, Chlamydia, Salmonella, Salmonella typhimurium, Salmonella Minnesota, Proteus mirabilis, Pseidomonas aeruginosa, Moraxella catarrhalis, Bordetella pertussis, Shigella, Klebsiella, and *Vibrio cholera,* which conserved portion is required to comprise the specific structure, GlcNAc-Hep2-phosphoethanolamine-KDO_2-LipidA. The claimed conjugate is further required to elicit a 'cross protective' immune response against heterologous strains of any of the generically recited 'gram negative bacteria'. The term 'gram negative bacteria' includes within its scope Gram negative cocci, Gram negative bacilli, aerobic Gram negative bacteria, and anaerobic Gram negative bacteria, both pathogenic and non-pathogenic. A review of the instant specification indicates that the first paragraph on page 15 and the last two paragraphs on page 8 of the specification describe an *Neisseria meningitidis* LPS from the specific strain, NMB-96, to be having the structure identified as 'GlcNAc-Hep2phosphoethanolamine-KDO_2-LipidA'. This specific meningococcal LPS having the specific chemical structure, when conjugated to a protein carrier, elicited LPS-specific antibodies that were 'cross reactive' with LPS from some heterologous strains of *Neisseria meningitidis.* Other than this, there is absolutely no showing that strains of *Neisseria gonorrhoeae, Haemophilus influenzae, nonptypeable Haemophilus influenzae, Haemophilus ducreyi, Helicobacter pylori, Escherichia coli, Chlamydia, Salmonella, Salmonella typhimurium, Salmonella minnesota, Proteus mirabilis, Pseidomonas aeruginosa, Moraxella catarrhalis, Bordetella pertussis, Shigella, Klebsiella,* and *Vibrio cholerae* contain an LPS having the specific conserved structure, GlcNAc-Hep2phosphoethanolamine-KDO_2-LipidA, which on conjugation to a protein carrier, before or after de-O-acetylation, elicits 'cross protective' immune response, cellular or humoral, against heterologous strains of any Gram negative bacteria, including those recited in the claims. The term 'cross protection' is not a part of the instant disclosure. There is absolutely no evidence that antigenic conjugates of the conserved structure of non-meningococcal origin, GlcNAc-Hep2phosphoethanolamine-KDO_2-LipidA, were produced and evaluated for cross-protectivity against even a single heterologous strain of a single Gram negative bacterium. No *in vivo* cross-protection data, or *in vitro* data correlative of *in vivo* cross-protection are provided.

The state of the art with respect to the development of a broadly protective LPS-based immunogenic composition against Gram negative bacterial pathogens reflects several problems. For example, with regard to the LPS of the Gram negative bacterial species, *Neisseria, or N.*

gonorrhoeae in particular, the state of the art documents structural heterogeneity or structural differences (see Lee *et al. Infect. Immun.* 63: 2508-2515, 1995; and John *et al. J. Biol. Chem.* 266: 19303-19311, 1991, both from Applicants' IDS). The state of the art further reflects the existence of intra- and inter-strain antigenic variations suggesting the gonococci's potential for reinfection and continued virulence (see lines 1-4 in column 2 of Rice *et al.*, US 6,099,839, published 8/8/2000). Rice *et al.* state (see the last two paragraphs in column 2):

> Ongoing attempts to develop an effective anti-gonococcal vaccine, however, have been plagued with several difficulties.
>
> Attempts to use individual surface components of the pathogen as targets for conventional vaccines have been **unsuccessful** because of their antigenic variability. Pilus vaccines have been protective only against infection with the homologous strain (used to make the pilus vaccine) and Por vaccination has been unsuccessful even in human experimental challenge. In addition, ***Neisseria gonorrhoeae*** **express marked phenotypic heterogeneity, typically shifting from one antigenic form to another at a frequency of >1 in 10^3 organisms ... making the surface of this organism a moving target for most vaccine strategies.** Although the vaccine candidates have provoked antibody responses, the antibodies and immune responses produced **have not been broadly protective**. [Emphasis added]

Gonococcal LPS or LOS is one such surface component, which undergoes constant antigenic variation. It is thus quite apparent from the above-identified post-filing art that induction of broad 'cross-protection' against heterologous strains gonococci, let alone any non-gonococcal Gram negative bacteria by a conjugate of a conserved portion of LPS of *Neisseria gonorrhoeae, Haemophilus influenzae, nonptypeable Haemophilus influenzae, Haemophilus ducreyi, Helicobacter pylori, Escherichia coli, Chlamydia, Salmonella, Salmonella typhimurium, Salmonella Minnesota, Proteus mirabilis, Pseudomonas aeruginosa, Moraxella catarrhalis, Bordetella pertussis, Shigella, Klebsiella*, and *Vibrio cholera,* has not been an unpredictable event. Even if one induced antibodies to gonococcal LPS or LOS, there is no predictability that the resultant antibodies elicited by one antigenic variant of a gonococcal LPS or LOS would recognize another antigenic variant of gonococcal LPS or LOS, let alone confer broadl 'cross-protection' against heterologous strains of any non-gonococcal Gram negative bacteria.

The various factors to be considered while determining whether or not a disclosure would require undue experimentation have been reiterated by the Court of Appeals in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 at 1404 (CAFC, 1988). It is emphasized that predictability or unpredictability is one of *Wands* factors. In the instant case, although the level of skill in the art is high, given the complex and incompletely understood areas of broadly cross-protective vaccines of

Gram negative bacterial surface components, such as, LPS/LOS, the specification lacks guidance, evidence, or working examples demonstrating that the conjugate as claimed was produced which indeed elicited 'cross-protection' against heterologous strains of any Gram negative bacteria, or heterologous strains of the same Gram negative bacteria from which the conserved portion was derived. Given the lack of *in vivo* cross protection data, or *in vitro* data correlative of *in vivo* cross-protection and what is known in the state of the art with regard to cross-protection among Gram negative bacteria, there is no predictability that the claimed product would elicit 'cross-protection' against heterologous strains of any Gram negative bacteria. In light of the art-recognized unpredictability in obtaining a broadly protective immune response and the existence phenotypic or antigenic heterogeneity, the lack of adequate disclosure and guidance, the breadth of the claims, and the unpredictability, identified in the relevant field, of the broadly protective function of the LPS/LOS antibodies, and the quantity of experimentation necessary, it is determined that undue experimentation would have been required to reproducibly practice the invention, as claimed.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

13) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

14) Claims 19-23 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, which Applicants regard as the invention.

(a) Claim 19 is incorrect in the recitation: 'Minnesota' and 'cholera' as opposed to --*minnesota*-- and --*cholerae*--.

(b) Claim 21 is vague and indefinite in the recitation 'fragments', because it is unclear what is encompassed in this limitation. What constitutes a 'fragment' and how much of the FHA's original structure has to be retained such that the resulting product can be considered as a 'fragment' is not clear. The metes and bounds of the structure encompassed in the limitation 'fragments' are indeterminate.

(c) Claim 23 is vague and indefinite in the recitation "effective amount" because it is a relative term. The term "effective" is not specifically defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art

would not be reasonably appraised of the scope of the claim. What amount qualifies as an 'effective' amount, and in what capacity the amount is 'effective', i.e., prophylactically effective, therapeutically effective etc., is unclear.

(d) Claims 20-23, which depends directly or indirectly from claim 19, are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, because of the indefiniteness or vagueness, identified above in the base claim.

Remarks

15) Claims 19-23 stand rejected.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

S. DEVI, PH.D.
PRIMARY EXAMINER

June, 2004